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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/254,623	07/08/1999	ELIZABETH SHANAHAN-PRENDERGAST	8009-7004-US	7303

7590 02/26/2002

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EXAMINER
DAVIS, MINH TAM B

ART UNIT	PAPER NUMBER
1642	20

DATE MAILED: 02/26/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/254,623	SHANAHAN-PRENDERGAST, ELIZABETH	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 January 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-124* is/are pending in the application.

4a) Of the above claim(s) *1-4,6-42,45,48-124* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5,43,44,46 and 47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Effective February 7, 1998, the Group Art Unit location has been changed, and the examiner of the application has been changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Minh-Tam Davis, Group Art Unit 1642.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Accordingly, claims 5, 43, 44, 46-47 are being examined.

The following are the remaining rejections.

RESTRICTION

Applicant argues that claims that depend on claim 5 cannot be subjected to a restriction requirement, because dependent claims by definition are not "independent". Claims, such as claim 45 and 57, which are withdrawn from consideration in view of an election of species must be examined upon determination that a generic claim, e.g. claim 5, is found to be allowable. In addition upon allowance of the generic claims, the Office is urged to review other pending claims again in order to consider the claims that can be readily considered without undue additional burdens.

In addition, Applicant asserts that the Office is not permitted to attempt to divide the subject matter of a generic claim on the basis of a restriction requirement or an election of species requirement, as evidenced by the case law *In re Weber, Soder*, and *Boksay*, and *Ex parte Holt* and *Randell*. Applicant further asserts that statement that

"claim 43 is examined only in the context of other therapeutically effective agents which are adjuvants, and not anti-inflammatory agent" ignores such precedent and is improper under US law.

Applicant's arguments set forth in paper No.19 have been considered but are not deemed to be persuasive for the following reasons:

The recitation of the case law *In re Weber, Soder*, and *Boksay*, and *Ex parte Holt* and *Randell* is acknowledged.

Claims 45 and 57 are not species of claim 5, in the context of a method for preventing neoplastic development, comprising administrating phospholipase A2 alone, because of the following reasons: 1) claim 45 is drawn to of a method for preventing neoplastic development, comprising administrating a venom, the structure and function of which are unrelated to phospholipase A2, 2) claim 47 is drawn to a method for preventing neoplastic development comprising administering an anti-inflammatory agent besides phospholipase A2, wherein an anti-inflammatory agent has a structure and function completely unrelated to phospholipase A2, and wherein the effect of an anti-inflammatory agent is completely distinct from the claimed anti-tumor development effect of phospholipase A2, and 3) Claim 5 is an improper implied Markush claim, since different members of the grouping are clearly structurally and functionally distinct.

MPEP 2173.05(h) provides that when the Markush group occurs in a claim reciting a process or a combination it is sufficient if the members of the group are disclosed in the specification to possess at least one property in common which is responsible for their function in the claimed relationship and it is clear from their very nature or from the prior art that all of them possess this

property. The members of the implied Markush groups recited in claim 5 do not share a common property, nor do they function by a common mechanism to prevent neoplastic development.

The requirement is still deemed proper and is therefore made FINAL.

Accordingly, claims 5, 43, 44, 46-47 are being examined, wherein claim 5 is examined only in the context of a method for preventing neoplastic development, comprising administrating phospholipase A2 alone.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, ENABLEMENT

Rejection under 35 USC 112, first paragraph of claims 5, 43, 44, 46-47 pertaining to lack of enablement for a method of preventing neoplastic development comprising administering phospholipase A2 remains for reasons already of record in paper No.17.

Applicant states that the arguments presented by the Examiner includes statements which relate to whether or not Applicant has proven that the present invention would be safe and effective. Applicant recites MPEP section 2107, subsection IV, arguing that the Office should not impose a 112, first paragraph rejection grounded on lack of utility basis unless a 101 rejection is proper. In particular, the factual showing needed to impose a rejection under 101 must be provided if a rejection under 112, first paragraph is to be imposed on lack of utility grounds.

Applicant asserts that the claimed invention is useful for preventing neoplastic development.

Applicant further asserts that a rejection cannot not be based on the requirement that Applicant "proves" that the invention works as disclosed. In addition, Applicant

recites MPEP 2107.01, *In re Gaubert*, and *In re Oetiker*, stating that the statement by the Examiner that "it is possible" that the invention might not work does satisfy the burden for making a rejection for lack of enablement. Documentary evidence should be cited to support factual conclusions. The Office must provide evidentiary support for its assertion that the invention would be totally incapable of providing any beneficial function.

In addition, Applicant asserts that it is not essential that the compound cures any condition, nor is it incumbent on Applicant to show that the invention would work in every situation, or that it would work on every patient.

Further, Applicant argues that the Statement by the Office that "the claims encompass a method for preventing neoplastic development from a normal human, without any tumor. The example in the specification only discloses the inhibition of growth of leukemic cells, or killing of leukemic cells that are injected into mice" does not statisfy the burden on the USPTO, because it does not provide a prima facie showing that the claimed invention lack utility, and it does not provide any evidentiary basis for factual assumption which could be relied upon in establishing a prima facie showing.

Concerning the statement by the Office that "it is unpredictable when and for how long one of skill in the art should administer the claimed phospholipase A2 for preventing cancer development", Applicant asserts that there is no requirement in order to satisfy the utility requirement for the duration of the treatment to be predictable. Delaying or showing neoplastic growth to any degree is such a useful result, and the

Office does not contain a showing that such usefulness cannot be obtained by the present invention.

Concerning the statement by the Office that " if phospholipase A2 is injected continuously during al the life span of human, severe side effects and toxicity could develop and thus preventing the success of the action of phospholipase A2, because several forms of phospholipase A2 are known to be toxic", Applicant asserts that there is no requirement that the invention be applied for an entire lifetime or a human in order to provide utility. Applicant recites MPEP 2107, *Atlas Powder v. E.I. DuPont De Nemours*, and *Ex parte Janin*, asserting that the Office should not construe 101 rejection under the logic of "practical" utility to require that that an applicant demonstrate that a therapeutic agent based on a claimed invention is safe or fully effective drug for human. In addition, it has been consistently and repeatly recognized that those of skill in the art would avoid activity that would be expected to produce harmful result. Further, it is not a function of the claims to specifically exclude possibly inoperative subject matter.

Concerning the statement by the Office that "the specification lacks guidance on dosage, frequency of treatment and assessment of disease progression in human", Applicant asserts that it is the ability of an artisan to determine suitable dosages. In addition, unless the PTO can establish that the invention as described would be totally incapable of producing any useful result, a rejection based on utility requirement is improper.

Concerning the statement by the Office that "the specification lacks description of how to assess human in risk of developing tumor, e.g. assessment based on family health history and genetic screening of said individual at risk of tumor development", Applicant asserts that it is not essential that the invention accomplish all its intended functions or operate under all conditions, or be capable of treating all patients at all times.

Concerning the statement by the Office that "it is unpredictable that phospholipase A2 alone would be able to kill starting tumor cells", Applicant asserts that it is not a requirement for patentability that it would have been "predictable" that the claimed invention would be successful. The Office has to provide evidentiary basis for factual assumption relied upon in establishing the prima facie showing. A mere allegation that the degree of efficacy of subject matter within an invention is unpredictable does not satisfy the burden on the USPTO.

Concerning the statement by the Office that "one of skill in the art would not have expected that phospholipase A2 alone could kill or prevent development of tumor mass from starting tumor cells", Applicant asserts that such requirement would be illogical, given that the present inventor is the first to describe the invention, and so it would be impossible for other of skill in the art to have any expectation as to the efficacy of the invention until the invention becomes known to them.

Concerning the statement by the Office that "in view of the above, undue experimentation would be required to practice the claimed invention", Applicant asserts that the Examiner has not shown that the invention would be incapable of providing any

useful result. The Examiner merely asserts that it would be her expectation that one would not be able to precisely predict the level of benefits provided to every patient by carrying out every regimen within the scope of the invention.

Applicant's arguments set forth in paper No.19 have been considered but are not deemed to be persuasive for the following reasons:

The recitation of MPEP 2107, subsection IV, MPEP 2107.01, and the case law *In re Gaubert*, *In re Oetiker* , *Atlas Powder v. E.I. DuPont De Nemours*, and *Ex parte Janin* is acknowledged.

Applicant not only does not directly answer several issues raised, but also misleadingly interpretes the Office assertions, and argues against several issues not stated by the Examiner.

Contrary to Applicant's assertion, the issue is not whether Applicant has "proven" that the present invention would be safe and effective, which is not suggested by the Office. In addition, the Office does not suggest that it is essential that the compound cures any condition, nor is it incumbent on Applicant to show that the invention would work in every situation, or that it would work on every patient. Further, the Office does not suggest that one would not be able to precisely predict the "level of benefits" provided to "every" patient by carrying out "every" regimen within the scope of the invention.

Moreover, the 112, first paragraph rejection is not grounded on lack of utility basis. In the previous Office action, all the following *Wands* factors have been carefully considered by the Office, when the 112, first paragraph, enablement rejection was

made: 1) The breadth of the claims, 2) The nature of the invention, 3) the state of the prior art, 4) The level of one of ordinary skill, 5) The level of predictability in the art, 6) The amount of direction provided by the inventor, 7) The existence of working examples, and 8) the quantity of experimentation needed to make or use in the invention based on the content of the disclosure. Thus, Applicant arguments that "unless the PTO can establish that the invention as described would be totally incapable of producing any useful result, a rejection based on utility requirement is improper" are not persuasive.

Concerning Applicant's arguments that the statement by the Examiner that "it is possible" that the invention might not work does satisfy the burden for making a rejection for lack of enablement, that documentary evidence should be cited to support factual conclusions and that the Office must provide evidentiary support for its assertion that the invention would be totally incapable of providing any beneficial function, Applicant argues against a sentence out of context. The Office has provided ample of reasons why the claims are rejected under 112, first paragraph, which are not answered by Applicant (see below). Similarly, concerning Applicant arguments that the Statement by the Office that "the claims encompass a method for preventing neoplastic development from a normal human, without any tumor. The example in the specification only discloses the inhibition of growth of leukemic cells, or killing of leukemic cells that are injected into mice" does not statisfy the burden on the USPTO, Applicant argues against a sentence out of the context. The Office has provided ample of reasons why

the claims are rejected under 112, first paragraph, which are not answered by Applicant (see below).

The Office agrees that there is no requirement that the invention be applied for an entire lifetime or a human in order to provide utility, that it has been consistently and repeatly recognized that those of skill in the art would avoid activity that would be expected to produce harmful result, and it is not a function of the claims to specifically exclude possibly inoperative subject matter. However, it is one alternative, albeit unlikely to be successful, when one cannot determine when and for how long one of skill in the art should administer the claimed phospholipase A2 for preventing cancer development.

Further, although it is the ability of an artisan to determine suitable dosages, however, in view of the unpredictability of phospholipase A2 to prevent neoplastic development, a certain guidance is required, as stated by MPEP 2164.03 (see discussion below).

Concerning the Office statement that the specification lacks description of how to assess human in risk of developing tumor, e.g. assessment based on family health history and genetic screening of said individual at risk of tumor development, contrary to Applicant assertion, this requirement does not mean that the invention has to accomplish all its intended functions or operate under all conditions, or be capable of treating all patients at all times. Without this assessment, one would not know which individual to administer the claimed phospholipase A2.

Concerning the statement by the Office that "it is unpredictable that phospholipase A2 alone would be able to kill starting tumor cells", and Applicant assertion that it is not a requirement for patentability that it would have been "predictable" that the claimed invention would be successful, contrary to Applicant assertion, the predictability of the art is one of the Wands factors based on which 112, first paragraph is rejected. Concerning Applicant arguments that the Office has to provide evidentiary basis for factual assumption relied upon in establishing the prima facie showing, and that a mere allegation that the degree of efficacy of subject matter within an invention is unpredictable does not satisfy the burden on the USPTO, the Office has provided ample of reasons why the claims are rejected under 112, first paragraph, which are not answered by Applicant (see below).

The unpredictability of using phospholipase A2 for preventing neoplastic develoment is high, and the amount of direction provided by Applicant is insufficient. Applicant has not answered to several following reasons stated by the Office explaining why the unpredictability of using phospholipase A2 for preventing neoplastic develoment is high, and why and the amount of direction provided by Applicant is insufficient:

1) Based on the example on pages 14-15 in the specification, one could not conclude that tumor development is prevented by a vaccine combination of venom and phospholipase A2. In the example on pages 14-15, mice are pretreated with a combination of venom and phospholipase A2 30 days before injection with of leukemic cells, and also received booster of the vaccine 12 or 15 days after the injection of

leukemic cells. Test mice are observed for extended life span after the death of the control mice, i.e. approximately 24 days after the injection of leukemic cells. Since the treated mice receive booster of the vaccine 12 or 15 days after the injection of leukemic cells, one would expect that said booster vaccine could contribute to killing leukemic cells. Applicant has not answered how one could determine, based on the example on pages 14-15, whether the vaccine prevents the development of leukemic cells or whether the vaccine actually kills leukemic cells rather than preventing development of cancer.

Further, there is no example, nor guidance in the specification on how to prevent neoplastic development by administration of phospholipase A2 alone, without venom.

Thus the amount of direction provided by the inventor is insufficient.

2) Moreover, the unpredictability of using phospholipase A2 alone for preventing neoplasm development is high for the following reasons recited in previous Office action, that have not been answered by Applicant. The claims are drawn to a method for preventing neoplasm development by injection of phospholipase A2 alone or together with an adjuvant, but not in combination with venom, as disclosed in the specification. It is unpredictable that phospholipase A2 alone would be able to kill starting tumor cells and consequently prevent development of tumor mass from starting tumor cells, because the tumor cell killing by a combination of a venom and phospholipase A2 as disclosed in an example on pages 14-15 could be due solely to the toxins in the venom, and not to phospholipase A2. It is known in the art that snake venom contains several toxins, such as atroporin, kaotree, crotoxin, that are able to selectively kill various types

of cancer cells both *in vitro* and *in vivo* (Lipss et al, PN=5,565,431 and Plata et al, PN=5,164,196). Further, one of skill in the art would not have expected that phospholipase A2 alone could kill or prevent development of tumor mass from starting tumor cells, due to either the cytotoxicity of the basic phospholipase A2 or the production of antibodies that suppress the activity of phospholipase A2, as suggested by the specification. Concerning killing of starting tumor cells due to the cytotoxicity of basic phospholipase A2, although basic phospholipase A2 when complexed with crotoxin A could selectively kill some tumor cells, one of skill in the art would have expected that the basic phospholipase A2 alone (or crotoxin B) would not be effective in killing tumor cells *in vivo*, because of non-specific absorption of the basic phospholipase A2 to many acidic tissue constituents in the absence of crotoxin A (Plata et al, of record, column 8, second paragraph). Moreover, concerning killing of starting tumor cells due to the production of antibodies against phospholipase A2 activity by administration of phospholipase A2, as suggested by the specification, there is no correlation between reduced phospholipase A2 activity and cancer development, because phospholipase A2 is only known to be a lipolytic enzyme that hydrolyzes the sn-2-acylester bond in glycerophospholipid. Although the specification discloses that elevated local and circulating levels of phospholipase A2 is a very early indication of neoplastic development prior to tumor mass (p.3, first paragraph), and that altered cytosolic phospholipase A2 activity or defects in its control and regulation is a predisposing factor to causing tumor cell development, Applicant has not shown that increased local and circulating levels of phospholipase A2 is responsible for tumor

development. Further, there is no data showing that altered cytosolic phospholipase A2 activity or defects in its control and regulation is a predisposing factor to causing tumor cell development. Moreover, even if altered cytosolic phospholipase A2 activity or defects in its control and regulation is a predisposing factor to causing tumor cell development, it is not clear what kind of alteration of cytosolic phospholipase A2 activity is referred to, and it is questionable that reduction of phospholipase A2 activity by anti-phospholipase A2 antibodies would alleviate the alteration of cytosolic phospholipase A2 activity or defects in its control and regulation. In addition, although anti-serum to venom could reduce phospholipase A2 activity, and anti-serum to venom could kill tumor cells, as disclosed by the specification, it is not necessary that the killing of tumor cells by anti-serum to venom is due to the presence of antagonist antibodies that reduce the activity of phospholipase A2 activity, because venom also comprises a complex mixture of many substances such as toxins, enzymes, growth factors, activators and inhibitors with wide spectrum of biological activities, and it is unpredictable which factors in the anti-venom serum is responsible for reduction of phospholipase A2 activity (Lipps et al, PN=5,565,431, of record, abstract and column 1, last paragraph). Further, it is well known in the art that there exist different types of antibodies, including agonists and antigonists, and thus injection of phospholipase A2 does not necessarily elicit the production of antagonist antibodies that reduce phospholipase A2 activity. The site of the activity of phospholipase A2 is not known, and it is unpredictable that said site is exposed such that antagonist antibodies against the activity of phospholipase A2 could bind to phospholipase A2, and inhibit its activity.

3) The breadth of the claim is overly broad. As written the claims encompass a method for preventing neoplastic development from a normal human, without any tumor. The example in the specification only discloses the inhibition of growth of leukemic cells, or killing of leukemic cells that are injected into mice, not preventing development of cancer from normal cells. The specification lacks description of how to assess human in risk of developing tumor, e.g. assessment based on family health history and genetic screening of said individual at risk of tumor development. Without this assessment, one would not know which individual to administer the claimed phospholipase A2. Further, the life span of human is much longer than that of mouse. Although in model rat and mouse, the time period when the animal, which is at risk of developing cancer, develops cancer is known, it is not the case in human. That is it is not known when a human who is at risk of developing cancer would start to develop cancer. Therefore, one cannot determine when and for how long one of skill in the art should administer the claimed phospholipase A2 for preventing cancer development. Furthermore, if phospholipase A2 is injected continuously during all the life span of human, severe side effects and toxicity could develop and thus preventing the success of the action of phospholipase A2, because several forms of phospholipase A2 are known to be toxic ((Menez et al, EP 0322262, 28/06/89, of record, Plata et al, PN=5,164,196, of record). Usually the toxicity data is not required, however if success of the action of phospholipase A2 is prevented by severe toxicity, such data is necessary.

MPEP 2164.03 teaches that "the amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability of the art. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The amount of guidance or direction refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to explicitly stated in the specification. In constrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as how to make and use the invention in order to be enabling." Yet the specification does not disclose any delay of tumor development by administering phospholipase A2. The specification lacks guidance as how to prevent cancer development in human at risk of developing said tumor or how to prevent cancer in patients who have had said tumor. That is the specification lacks guidance on dosage, frequency of treatment and assessment of disease progression in human. Although it is the ability of an artisan to determine suitable dosages, however, in view of the unpredictability of phospholipase A2 to prevent neoplastic development, a certain guidance is required, as stated by MPEP 2164.03. Furthermore, the specification lacks description of how to assess human in risk of developing tumor, e.g. assessment based on family health history and genetic screening of said individual at risk of tumor development. Without this assessment, one would not know which individual to administer the claimed phospholipase A2.

In view of the fact that 1) the breadth of the claim is overly broad, 2) the lack of sufficient guidance in the specification on dosage and necessary schedule, and working examples on how to successfully prevent tumor *in vivo* using the claimed phospholipase A2, and 3) the unpredictability of preventing cancer development by phospholipase A2, and further in view of the complex nature of the invention, it would have been undue experimentation for one of skill in the art to practice the claimed invention. Thus, contrary to Applicant assertion, it is not illogical or unreasonable to conclude that based on the disclosure in the specification, the unpredictabity of the art, and the complex nature of the invention, one of skill in the art would not have expected that phospholipase A2 alone could kill or prevent development of tumor mass from starting tumor cells".

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, SCOPE

1. Rejection under 35 USC 112, first paragraph of claims 5, 43, 44, 46-47 pertaining to lack of enablement for a method of preventing neoplastic development comprising administering part of phospholipase A2 remains for reasons already of record in paper No.17.

Applicant argues that as noted above, there is no requirement that one is able to predict the level of efficacy of each embodiment within the invention. Applicant recites *In re Fuetterer*, arguing that 112, first paragraph does not require that Applicant discovers and describe which subject matter within a generic group of component function

properly in accordance with the invention, and the precise extent of their efficacy.

Applicant further argues that an example is not required in the specification.

Applicant's arguments set forth in paper No.19 have been considered but are not deemed to be persuasive for the following reasons:

The Examiner does not suggest that it is required that one is able to predict the "level of efficacy" of each embodiment within the invention. The Office states that it is unpredictable that "part" of phospholipase A2 would be useful for preventing neoplastic development, in view of 1) the lack of the description in the specification which part of phospholipase A2 would produce antibodies that are antagonist to phospholipase A2 and bind to phospholipase A2, and 2) the unpredictability that part of phospholipase A2, which could produce antibodies that are antagonist to phospholipase A2, is exposed on the surface of phospholipase A2, such that said antibodies could bind to phospholipase A2.

MPEP 2164.03 teaches that "the amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability of the art. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The amount of guidance or direction refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to explicitly stated in the specification. In constrast, if little is known in the prior art

about the nature of the invention and the art is unpredictable, the specification would need more detail as how to make and use the invention in order to be enabling.

The claims encompass a method of preventing neoplastic development comprising administering part of phospholipase A2, which is a specific epitope of phospholipase A2, wherein said epitope could produce antibodies that are antagonistic and bind to phospholipase A2. Since it is unpredictable that there exists a specific epitope which could produce antibodies that are antagonistic and bind to phospholipase A2, and since little is known in the prior art about the nature of the invention, the specification would need more detail as how to make and use the invention in order to be enabling, as taught by MPEP 2164.03. The specification however lacks information concerning the structure and properties of the claimed part of phospholipase A2, or specific epitope of phospholipase A2, wherein said epitope could produce antibodies that are antagonistic and bind to phospholipase A2. The specification does not decribe whether the claimed epitope is linear or requires 3-dimensional structure, as taught by Herbert et al (of record). The specification does not disclose the boundaries of the claimed epitope, which are not easy to define, as taught by Greenspan et al (of record).

Further, for part of phospholipase A2 to prevent neoplastic development, it would require that said part of phospholipase A2 produces antibodies that are antagonistic and bind to phospholipase A2, i.e. a specific epitope of phospholipase A2 with specific properties, the existence of which is unpredictable. Thus, although part of phospholipase A2 is a species within the generic whole length phospholipase A2, since the existence of said species is unpredictable, the claims are not enabled.

2. Rejection under 35 USC 112, first paragraph of claims 5, 43, 44, 46-47 pertaining to lack of enablement for a method of preventing neoplastic development comprising administering any type of phospholipase A2 remains for reasons already of record in paper No.17.

Rejection remains because Applicant has not answered this issue.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 703-305-2008. The examiner can normally be reached on 9:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, ANTHONY CAPUTA can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-

872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0916.

MINH TAM DAVIS

February 21, 2002

ANTHONY C. CAPUTA
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600